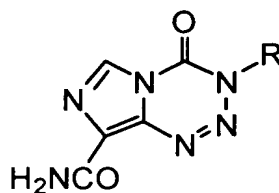


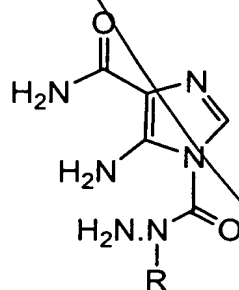
What is claimed is

1. A process for the preparation of a compound of the formula IA



IA

wherein R is an alkyl group having from 1 to 6 carbon atoms, which comprises reacting a compound of the formula II



II

wherein R is described above, with an oxidation/cyclization agent in the presence of an iodide, in an inert medium, under an inert atmosphere and at a temperature and for a time sufficient enough to produce a compound of the formula IA, wherein said iodide is soluble in said inert medium.

2. The process of claim 1 wherein R is an alkyl group having 1 to 4 carbon atoms.

3. The process of claim 1 wherein said oxidation/cyclization agent is selected from the group consisting of:

- a) periodic acid,
- b) iodine/potassium iodate,
- c) bromine,

- d) chlorine; and
- e) a reagent that oxidizes NH_2 to NZ , where Z represents, Oxygen, (H, Hal), or Hal_2 , and wherein Hal is chlorine, bromine or iodine.

4. ~~The process of claim 1 wherein said iodide is a quarternary ammonium iodide and said inert medium is an inert organic solvent.~~

5. The process of claim 4 wherein said iodide is selected from the group consisting of Bu_4NI and KI .

6. ~~The process of claim 4 wherein said inert organic solvent is selected from the group consisting of:~~

- ~~a) an amide;~~
- ~~b) an acyclic ether;~~
- ~~c) a cyclic ether;~~
- ~~d) an alkyl alkanoate wherein the alkyl group has 1 to 4 carbon atoms and the alkanoate group has 2 to 4 carbon atoms;~~
- ~~e) a halogenated hydrocarbon and~~
- ~~f) mixtures thereof.~~

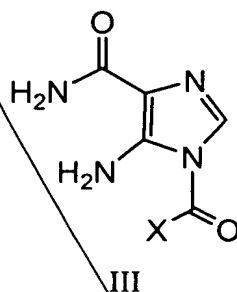
7. The process of claim 6 wherein the organic solvent is selected from the group consisting of:

- a) DMF;
- b) t-butyl-methyl ether;
- c) THF;
- d) acetonitrile;
- e) methylene chloride;
- f) toluene; and
- g) mixtures of the above solvents,

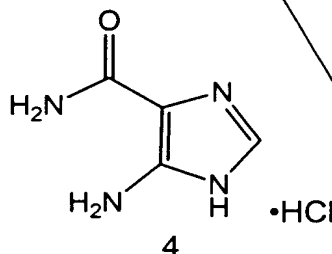
8. The process of claim 7 wherein the reaction takes place at a temperature of about $(-)$ 20°C to about $(+)$ 70°C and under a nitrogen atmosphere.

9. The process of claim 6 wherein:
- a) the organic solvent is a 50/50 mixture of THF/CH₃CN;
 - b) the oxidation/cyclization agent is H₅IO₆;
 - c) the iodide is Bu₄NI and
 - d) the reaction takes place at a temperature of about 0°C to about 60°C.

10. A process for preparing a compound of the formula III:



which comprises reacting a compound of the formula 4:



with a compound of the formula X-CO-Y, wherein each of X and Y is the same or different leaving group, to yield a compound of the formula III.

11. The process of claim 10 wherein X of said compound X-CO-Y is selected from the group consisting of

- a) phenyloxy;
- b) 2-naphthyloxy and
- c) substituted phenyloxy,

and wherein Y of said compound X-CO-Y is selected from:

- a) chlorine,
- b) bromine, or

c) iodine.

12. The process of claim 11 wherein the substituents on said substituted phenoxy group are selected from the group consisting of:

- a) nitro;
- b) pentafluoro;
- c) chlorine;
- d) bromine;
- e) iodine, and
- f) combinations of the above.

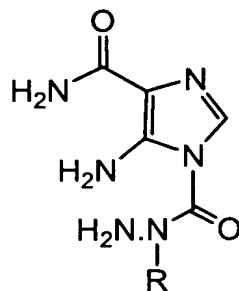
13. The process of claim 10 wherein said reaction of the compound of the formula 4 with a compound of the formula X-CO-Y is performed in the presence of an acid binding agent, in an inert organic solvent, under an inert atmosphere and at a temperature of about (-) 20°C to about (+) 50°C.

14. The process of claim 13 wherein said acid binding agent is a tertiary amine.

15. The process of claim 13 wherein the organic solvent is selected from the group consisting of

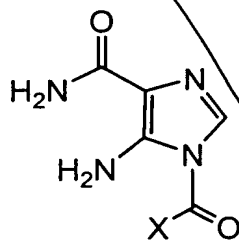
- a) an amide;
- b) an acyclic ether;
- c) a cyclic ether;
- d) an alkyl alkanoate wherein the alkyl group has 1 to 4 carbon atoms and the alkanoate group has 2 to 4 carbon atoms;
- e) a halogenated hydrocarbon; and
- f) mixtures thereof.

16. A process for the preparation of a compound of the formula II:



II

wherein R is an alkyl group having from 1 to 6 carbon atoms, comprising, reacting a compound of the formula III:



III

wherein X is a leaving group of the type that activates its adjacent carbonyl group towards nucleophiles, with an alkylhydrazine having from 1 to 6 carbon atoms.

- 15 17. The process of claim 16 wherein said alkylhydrazine is R-NH-NH₂, wherein R is an alkyl group having 1 to 4 carbon atoms.

18. The process of claim 16 wherein the reaction takes place in an inert organic solvent selected from the group consisting of:

- a) a non-nucleophilic amine and
b) an ether; and
c) mixtures thereof.

Sub
B2

5

10

20

19. The process of claim 16 wherein X is selected from the group consisting of:

- a) phenoxy;
- b) 2-naphthyloxy and
- c) substituted phenoxy, wherein the substituents are electron withdrawing.

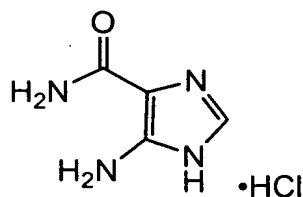
20. The process of claim 19 wherein said substituents are selected from the group consisting of:

- a) 2-nitro;
- b) 4-nitro;
- c) pentafluoro;
- d) chlorine and
- e) bromine.

21. The process of claim 17 wherein said alkylhydrazine is a 1-alkyl derivative of 5-amino-4-(aminocarbonyl)-1H-imidazole-1-carboxylic acid hydrazide wherein the alkyl group contains 1 to 6 carbon atoms.

22. The process of claim 21 wherein said alkylhydrazine is 5-amino-4-(aminocarbonyl)-1H-imidazole-1-carboxylic acid 1-methylhydrazide.

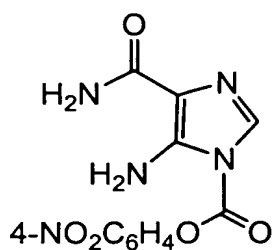
23. The process of claim 14 wherein compound 4:



4

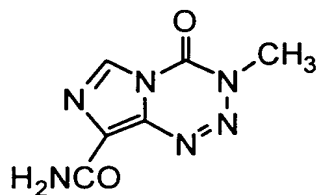
is reacted with 4-nitrophenyl chloroformate, in the presence of triethyl amine, said reaction taking place in methylene chloride solvent, under a nitrogen atmosphere and at a temperature of about (-)20°C to about (+) 50°C to yield compound (3):

21



(3)

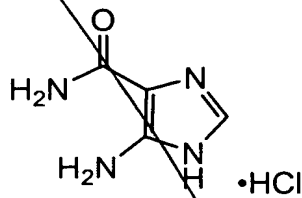
24. A process for preparing temozolomide (1):



(1)

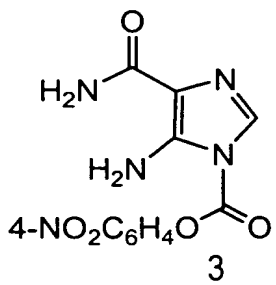
comprising:

a) reacting compound 4:



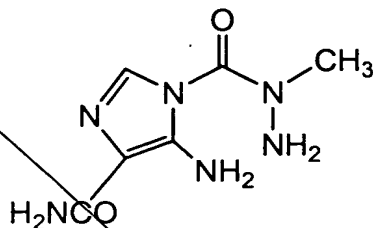
(4)

with 4-nitrophenyl chloroformate in the presence of triethylamine in CH_2Cl_2 , under a nitrogen atmosphere at about 25°C to obtain compound (3):



3 ;

b) reacting compound (3) with methylhydrazine in DMF at about 0°C to obtain compound (2):

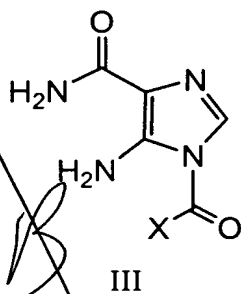


(2)

, and

c) reacting compound (2) with Bu_4NI in a 50/50 mixture of THF/ CH_3CN , at a temperature of about (+) 60°C for a time of about zero to sixty minutes, followed by the cooling of the reaction mixture to about (+) 25°C and the addition of H_5IO_6 and stirring for about 10 to about 60 minutes to obtain temozolomide (1).

25. A compound of the formula:

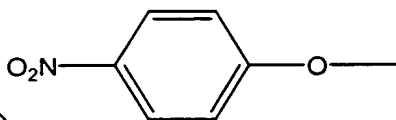


III

or an active ester thereof, wherein X is a leaving group of the type that activates its adjacent carbonyl group towards nucleophiles.

26. The compound of claim 25 wherein X is OH, said compound being 5-amino-4-(aminocarbonyl)-1H-imidazole-1-carboxylic acid.

27. ~~The compound of claim 25 wherein X is~~



said compound being 1-(4-nitrophenyl)-5-amino-4-(aminocarbonyl)-1H-imidazole-1-carboxylate.

5

28. The compound of claim 25 wherein X is $\text{-N(CH}_3\text{)-NH}_2$, said compound being 5-amino-4-(aminocarbonyl)-1H-imidazole-1-carboxylic acid-1-methylhydrazide.

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